Case Report

Pacemaker surgical site infection caused by *Mycobacterium goodii*

Hélène Marchandin,^{1,2} Pascal Battistella,³ Brigitte Calvet,³
Hélène Darbas,¹ Jean-Marc Frapier,³ Hélène Jean-Pierre,^{1,2} Sylvie Parer,⁴
Estelle Jumas-Bilak,² Philippe Van de Perre^{1,5} and Sylvain Godreuil^{1,5}

Correspondence
Sylvain Godreuil
godreuil@yahoo.fr

¹Centre Hospitalier et Universitaire de Montpellier, Laboratoire de Bactériologie, F-34295 Montpellier, France

²Université Montpellier 1, EA3755, Faculté de Pharmacie, Laboratoire de Bactériologie-Virologie, F-34060 Montpellier, France

³Centre Hospitalier et Universitaire de Montpellier, Service de Chirurgie Thoracique et Cardio-Vasculaire, F-34295 Montpellier, France

⁴Centre Hospitalier et Universitaire de Montpellier, Service d'Hygiène Hospitalière, F-34295 Montpellier, France

⁵Université Montpellier 1, EA 4205, F-34000 Montpellier, France

We describe what we believe to be the first documented case of *Mycobacterium goodii* infection in Europe. It is also the second documented report of a pacemaker pocket surgical site infection caused by *M. goodii*. Although rarely involved in such infections, rapidly growing mycobacteria should be recognized during conventional bacteriological investigations and further identified by molecular tools to provide adequate therapy. In the present case, antimicrobial therapy with doxycycline without removal of the pacemaker was successful.

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Introduction

The rapidly growing mycobacteria (RGM) species involved in human disease primarily belong to the *Mycobacterium fortuitum* group, the *Mycobacterium chelonae/abscessus* group, and the *Mycobacterium smegmatis* group (Brown-Elliott & Wallace, 2002). *Mycobacterium goodii* was recognized in 1999 among the *M. smegmatis* group, which also includes *M. smegmatis sensu stricto* and *Mycobacterium wolinskyi* (Brown *et al.*, 1999). Here we describe what we believe to be the first documented *M. goodii* infection reported in Europe.

Case report

A 23-year-old man was admitted to the Montpellier University Hospital for severe mitral and tricuspid valve insufficiency and atrioventricular block. His past medical history included partial atrioventricular canal defect repair at the age of 5 years. He underwent a mechanical double valve replacement with definitive epicardial pacemaker implantation under antibiotic prophylaxis with cefamandole (1.5 g during anaesthetic induction and 750 mg every

2 h during the surgical procedure). On postsurgical day 8, the patient was febrile (38.5 °C) and three blood cultures were taken. An increased total white blood cell count (14.7×10^3 cells mm⁻³) with 81 % polymorphonuclear leukocytes and a C-reactive protein (CRP) level of 96 mg l⁻¹ were noted. Blood cultures remained negative and no antibiotic treatment was started. On day 13, spontaneous disunion of the abdominal wound associated with the pacemaker pocket was observed and the purulent discharge was analysed on 3 consecutive days. The transoesophageal echocardiogram showed no evidence of endocarditis. On day 13, a combination of intravenous linezolid (600 mg twice daily) and ofloxacin (200 mg twice daily) was started, and on the following 2 days the patient became afebrile, and a serous discharge from the wound was observed. Gram-staining of the samples revealed rare polymorphonuclear leukocytes but no organism. After 3 days of incubation at 37 °C, the three samples yielded the growth of an irregular Gram-positive, rod-shaped and strictly aerobic organism recovered in pure culture on Columbia sheep blood agar. Catalase production was noted, and an acid-fast stain of the isolates revealed acid-fast bacilli. A smear for acid-fast bacilli was then performed on the three pus samples, which revealed organisms consistent with mycobacteria for one of them. After subculture on Middlebrook medium, growth of smooth nonpigmented colonies was noted within 3 days. A commercial multiplex

Abbreviations: CRP, C-reactive protein; RGM, rapidly growing mycobacteria.

The GenBank/EMBL/DDBJ accession number for the partial 16S rRNA gene sequence of the *Mycobacterium goodii* isolate is EU868812.

line probe assay, GenoType Mycobacterium AS (Hain Lifescience), identified the organism as *Mycobacterium goodii*. A partial 16S rRNA gene sequence of 754 bp was determined (Telenti *et al.*, 1993) (GenBank accession no. EU868812). Using the BLAST (Basic Local Alignment Search Tool) program (Altschul *et al.*, 1997), sequence identity levels of 100% and 99.7% were observed with *M. goodii* ATCC 700504^T (GenBank accession no. AY457079) and *M. smegmatis* ATCC 19420^T (GenBank accession no. AY457078), respectively. Signature nucleotides previously described by Brown *et al.* (1999) as species-specific in the 16S rRNA gene were identical to those of the *M. goodii* sequence. The *in vitro* antibiotic susceptibility of the isolate was tested using commercially manufactured broth micro-dilution panels (Trek Diagnosis Systems). The results (Table 1) were interpreted according to the guidelines of the Clinical and Laboratory Standards Institute (Woods *et al.*, 2003).

On day 19, apyrexia remained, the CRP level decreased to 37 mg l⁻¹, and the white blood cell count was within normal ranges (6.3×10^3 cells mm⁻³); the antimicrobial therapy was switched to intravenous ofloxacin (200 mg twice daily) and amikacin (1 g daily). On day 31, amikacin was replaced with oral cotrimoxazole (sulfamethoxazole 800 mg/trimethoprim 160 mg twice daily), which was rapidly discontinued because of an increased blood creatinine level of 180 µmol l⁻¹ and replaced with doxycycline (100 mg twice daily). The pacemaker was not removed because of the major risk involved in a third surgical procedure. Furthermore, neither mediastinal nor pacing leads were clinically infected. The patient was discharged on day 61. Two months after surgery, the pacemaker pocket had healed and the same antimicrobial therapy was prolonged for an additional 4 months. At the most recent follow-up (6 months after stopping antibiotic

therapy), the patient was doing well, with no fever episodes, with a blood cell count of 7×10^3 cells mm⁻³, a CRP level of 5.6 mg l⁻¹, and a totally cold and healed pacemaker pocket.

Analysis of perioperative-related risk factors for this patient showed no comorbidities. The patient was admitted to the unit the day before surgery. The preparation of the patient's skin with povidone-iodine as well as antibiotic prophylaxis with cefamandole were reviewed and had been appropriately conducted according to national guidelines. The surgical procedure was much longer than the recommendations (595 min vs 240 min) but it was a redo intervention. The patient was kept in the intensive care unit for a short period of time (2 days) and all the invasive catheters were removed on day 2 when the patient was transferred to the ward unit.

Environmental investigations were reviewed and conducted to search for a potential source of infection. One month before this case, the operating room had undergone an annual environmental screening by air, surface and water sampling. Forty-five air samples cultured on blood agar under conditions allowing the detection of RGM were negative for mycobacteria. Twenty surface and water samples yielded negative cultures except for *Pseudomonas putida* cultured from water used to fill warming mattresses. Two other water samples were collected from the mattresses after the *M. goodii* infection diagnosis. Mycobacterial growth remained negative on Löwenstein-Jensen, Middlebrook 7H11 and Columbia sheep blood agar media. Water samples were negative for mycobacterial DNA by 16S rRNA gene amplification followed by Temporal Thermal Gel Electrophoresis (Roudiere *et al.*, 2007) and by specific amplification of the *hsp65* gene (Telenti *et al.*, 1993).

Table 1. *In vitro* susceptibility of *Mycobacterium goodii* isolated in this study and comparison with data reported previously (Brown *et al.*, 1999)

Drug	Our report			Data from Brown <i>et al.</i> (1999)	
	MIC (µg ml ⁻¹)	Breakpoints used*	Interpretation†	MIC ₉₀ ‡ (µg ml ⁻¹)	MIC range (µg ml ⁻¹)
Amikacin	2	≤16/≥64	S	≤1	≤0.25–4
Tobramycin	0.5	≤4/≥16	S	8	≤0.5–8
Ciprofloxacin	0.25	≤1/≥4	S	0.5	≤0.063–1
Gatifloxacin	0.06	≤2/≥8	S	ND	ND
Minocycline	0.12	≤1/≥16	S	ND	ND
Doxycycline	ND	≤1/≥16	ND	0.5	≤0.25–1
Linezolid	1	≤8/≥32	S	ND	ND
Imipenem	2	≤4/≥16	S	8	≤0.5–8
Cefoxitin	64	≤16/≥128	I	>256	≤8–>256
Clarithromycin	32	≤2/≥8	R	>128	≤0.25–>128
Sulfamethoxazole–trimethoprim	0.25	≤32/≥64	S	8	≤1–8

ND, Not determined.

*Breakpoints from Brown *et al.* (1999). Minocycline was interpreted according to breakpoints for doxycycline.

†S, Susceptible; I, intermediately susceptible; R, resistant.

‡MIC₉₀, MIC which inhibits 90% of the strains.

Discussion

Diagnosis of RGM infections may be difficult; conventional methods may lead to inconclusive identification, and previous reports also suggest that they can be erroneously identified as contaminant Gram-positive bacilli (Sharma *et al.*, 2005; Siu *et al.*, 2005). Although several phenotypic characteristics can assist in the identification of *M. goodii* (Brown *et al.*, 1999), they do not present a strong discriminating power in differentiating *M. goodii* from other members of the *M. smegmatis* group; the accurate identification of *M. goodii* is therefore based on unique mycolic acid and PCR-restriction enzyme patterns and the 16S rRNA gene sequence (Brown *et al.*, 1999). In the present case, the line probe assay and partial 16S rRNA gene sequencing contributed to *M. goodii* identification.

Using molecular tools, Brown *et al.* (1999) characterized the first 28 isolates of *M. goodii*, eight of which had been previously reported as *M. smegmatis* group isolates. These isolates were mainly involved in community-acquired wound/bone infections and respiratory and nosocomial diseases, and among the latter, two cases of infected pacemaker site were identified but not further documented (Brown *et al.*, 1999). Since the index tabulation of cases by Brown *et al.* (1999), a few additional cases of human *M. goodii* infection have been reported, including olecranon bursitis, hernia mesh infection (Friedman & Sexton, 2001; Sohail & Smilack, 2004), endophthalmitis (Spencer *et al.*, 2005) and the first nosocomial outbreak of *M. goodii* wound infections associated with surgical implants other than the pacemaker (Ferguson *et al.*, 2004). Toda *et al.* (2006) reported the isolation of *M. goodii* from pacemaker leads in a patient with bloodstream infection after left thorax injury.

To our knowledge, the present case is the fourth reported and the second documented case of pacemaker site infection caused by *M. goodii*, the first being recently documented by Chrissoheris *et al.* (2008). No pacemaker site infection caused by the other two species of the *M. smegmatis* group has been described so far. Moreover, RGM remain unusual causes of pacemaker site infection, with roughly a dozen cases reported in the literature that involve *M. abscessus*, *M. fortuitum*, *M. chelonae*, *M. massiliense* and *M. goodii* (Chrissoheris *et al.*, 2008; Giannella *et al.*, 2007; Simmon *et al.*, 2007; Siu *et al.*, 2005). The present case is, to our knowledge, the first documented *M. goodii* infection reported in Europe since a large majority of previously reported cases originated in the United States, the remaining being from Australia, Canada and Japan (Brown *et al.*, 1999).

Among the pre-, intra- and postoperative risk factors for surgical site infection (SSI), the 9.55 h duration of surgery for this patient should be highlighted. Time beyond which there is a risk factor for surgical SSI is 4 h, and the longer surgery lasts, the more environmental exposure there is, and therefore a higher infection rate is expected (Ku *et al.*, 2005).

The ecological niche of *M. goodii* remains unclear although *M. goodii* is also recognized as a pathogen for dogs and the spotted hyena (Bryden *et al.*, 2004; van Helden *et al.*, 2008).

However, the patient and the members of the surgical team had had no contact with animals before surgery. By comparison with other RGM, the environment could be considered the most probable reservoir but environmental investigations were unsuccessful in tracing the patient's infection source despite extensive screening, as was the case during the outbreak described by Ferguson *et al.* (2004). To date, no other isolate of this species has been identified in our hospital.

One important feature distinguishing the *M. smegmatis* group from the other RGM groups is its general lack of susceptibility to clarithromycin. The *in vitro* susceptibility data observed for *M. goodii* in this study are consistent with previously reported susceptibility data (Brown *et al.*, 1999; Friedman & Sexton, 2001; Sohail & Smilack, 2004). As in other RGM infections, treatment success depends on the nature and gravity of the disease, oral single-drug therapy being effective for localized infections, whereas a combination of oral and intravenous antimicrobial drugs is required for more severe disease (Brown *et al.*, 1999). Moreover, in the case of pacemaker infection, removal of the pacemaker system is crucial because of the high rate of uncontrolled or relapsing bacteraemia, even after prolonged antimicrobial therapy (Marschall *et al.*, 2007). In the present case, the initial treatment was based on general policies for the management of pacemaker infection caused by common pathogens and switched to a combination of intravenous drugs effective on RGM when mycobacterial infection was diagnosed. However, the pacemaker was not removed in this fragile patient and 6 months after antibiotic treatment no relapsing infection has been observed. At the time of infection, no data were available on optimal treatment of pacemaker site infection caused by *M. goodii*. Since then, Chrissoheris *et al.* (2008) have reported successful treatment of this infection by removal of the pacemaker and 8 weeks of trimethoprim-sulfamethoxazole therapy. More generally, among the few cases of pacemaker site infection due to RGM, antimicrobial therapy including one or a combination of two drugs was given for 1–6 months and was associated with the removal of the pacemaker in all cases except one involving *M. fortuitum* (Giannella *et al.*, 2007; Simmon *et al.*, 2007; Siu *et al.*, 2005). In this latter case, the patient was given ciprofloxacin in association with clarithromycin for 6 weeks with no relapsing infection (Pastor *et al.*, 2006).

In conclusion, we describe the second documented case of pacemaker site infection caused by *M. goodii*. RGM remain infrequently involved in pacemaker infections but their role may be underestimated. To avoid any delay in diagnosis, clinicians and microbiologists should be aware of RGM as potential causes of surgical site and material infections. Molecular identification methods remain essential for rapid diagnosis and for guiding prompt and adequate antimicrobial therapy.

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